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Hazard/Risk Assessment

PROBABILISTIC RISK ASSESSMENT OF COTTON PYRETHROIDS: I. DISTRIBUTIONAL ANALYSES OF LABORATORY AQUATIC TOXICITY DATA

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Abstract—This is the first in a series of five papers that assess the risk of the cotton pyrethroids in aquatic ecosystems in a series of steps ranging from the analysis of effects data through modeling exposures in the landscape. Pyrethroid insecticides used on cotton have the potential to contaminate aquatic systems. The objectives of this study were to develop probabilistic estimates of toxicity distributions, to compare these among the pyrethroids, and to evaluate cypermethrin as a representative pyrethroid for the purposes of a class risk assessment of the pyrethroids. The distribution of cypermethrin acute toxicity data gave 10th centile values of 10 ng/L for all organisms, 6.4 ng/L for arthropods, and 380 ng/L for vertebrates. For bifenthrin, cyfluthrin, lambda-cyhalothrin, and deltamethrin, the 10th centile values for all organisms were 15, 12, 10, and 9 ng/L, respectively, indicating similar or somewhat lower toxicity than cypermethrin. For tralomethrin and fenpropathrin, the 10th centiles were <310 and 240 ng/L, respectively. The distribution of permethrin toxicity to all organisms, arthropods, and vertebrates gave 10th centiles of 180, 76, and 1600 ng/L, respectively, whereas those for fenvalerate were 37, 8, and 150 ng/L. With the exception of tralomethrin, the distributions of acute toxicity values had similar slopes, suggesting that the variation of sensitivity in a range of aquatic nontarget species is similar. The pyrethroids have different recommended field rates of application that are related to their efficacy, and the relationship between field rate and 10th centiles showed a trend. These results support the use of cypermethrin as a reasonable worst-case surrogate for the other pyrethroids for the purposes of risk assessment of pyrethroids as a class.

Keywords—Risk assessment Pyrethroids Cotton Aquatic Toxicity

INTRODUCTION

Cotton pyrethroid insecticides include bifenthrin, cyfluthrin, cypermethrin, deltamethrin, esfenvalerate, fenpropathrin, lambda-cyhalothrin, permethrin, and tralomethrin. Growers use these compounds to control insect pests such as heliothine Lepidoptera (boll and army worms), Pentatomidae (stink bugs), and thrips. Properly used, pyrethroids have been a major contributor to improved cotton yields over the last two to three decades. Despite their high efficacy and generally low mammalian toxicity, concerns have existed regarding potential risks to aquatic organisms, particularly fish and arthropod invertebrates, because of high toxicity observed in standard laboratory studies. However, it has also been widely recognized that exposure of aquatic organisms under field conditions would be significantly reduced through the tendency of pyrethroids to bind rapidly and extensively to suspended particulate matter, sediments, and aquatic plants [1–3].

Companies seeking to register pyrethroid products have conducted many higher-tier regulatory studies to quantify the extent of this reduced risk. These have included farm pond monitoring studies near cotton fields treated with pyrethroids, large-scale pond mesocosm studies comparing pyrethroid-treated ponds with untreated controls, large-scale runoff studies measuring pyrethroid transport into farm ponds, small-scale simulated runoff studies evaluating edge of field losses under controlled conditions, and research into the bioavailability and toxicity of pyrethroids adsorbed to sediments and their adsorption kinetics. In addition to these regulatory studies, pyrethroids have been intensively studied by the wider scientific community. Therefore, an abundance of data exists with which to evaluate these compounds.

In addition to generating higher-tier data, registrants have been required to modify pyrethroid use labels to mitigate the perceived risk to aquatic ecosystems. Label restrictions include 25- and 150-ft no-spray distances for ground and aerial applications, respectively, when used directly adjacent to water courses. Other recommendations to reduce spray drift and runoff (thereby reducing exposure) also have been added to the use labels to promote safe uses.

In this and the four following papers [4–7], a probabilistic risk assessment was conducted to consolidate the data and to account for label mitigation factors. The risk assessment reviewed existing data from toxicity tests and field studies and used state-of-the-art approaches to generate landscape-scale exposure evaluations. The risk assessment was conducted using cypermethrin as the representative compound of the pyrethroid class as a whole.

We present the work in a series of five papers. This first paper synthesizes single-species toxicity data for aquatic organisms using distributional approaches and assesses the suitability of cypermethrin as a representative of this class of pyrethroids. The second paper [4] evaluates field studies that support and extend the information on potential ecological effects of pyrethroids in relation to effects observed in laboratory studies. The third paper [5] describes a landscape analysis of a cotton-producing county (Yazoo County, MS, USA) and quantifies landscape factors that influence exposure of

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aquatic systems to pyrethroids. The fourth paper [6] incorporates the results of the landscape analysis into a refined exposure assessment. The final paper [7] combines the effects and exposure assessments into a characterization of risk to aquatic life.

Risk assessment

The Aquatic Risk Assessment and Mitigation Dialogue Group [8] suggested that four tiers be used in the risk assessment process for pesticides in aquatic ecosystems. Tier I was a simple worst-case estimation of environmental concentration, which was compared with the effect level for the most sensitive species (the hazard quotient approach). If this hazard quotient suggested a potential hazard, further tiers of risk assessment with more realistic and more complete exposure and effects data could be used for the assessment. The report [8] suggested that tiers II and III of the assessment process make use of probabilistic approaches, whereas the highest tier (tier IV) could include specially designed toxicity tests (mesocosms, field tests, and so on) as well as assessments based on landscape models. Use of these and other assessment tools has also been suggested in the final draft reports of the ECOFRAM process [9]. Although this assessment followed the general approaches that have been suggested in the literature [10–12], the major focus was on refining the characterization of effects and exposure in a specific use pattern—on cotton. The extensive descriptions of the general use patterns, physicochemical properties, ecosystems at risk, and so on, that would normally be included in a problem formulation have been discussed elsewhere [2,3,13].

Because of the toxicity of pyrethroids to aquatic arthropods and the high estimations of environmental exposures in tier I, all the pyrethroids move to higher tiers for further assessment. Failure of tier I does not indicate that the use of the pyrethroids presents an unacceptable risk in the environment, but rather that a degree of concern exists that justifies the implementation of more refined (higher) tiers of risk assessment.

Distributional analyses of toxicity and exposure data that are similar to those suggested in tiers II and III above have been applied to risk assessments in a number of situations [14–19]. They are a useful method for characterizing the range of toxicity of a substance and the range of exposures that may be found in the environment, as well as for risk prioritization and assessment [8–11].

The use of distributional analysis techniques in probabilistic risk assessment is facilitated when larger data sets are available. Toxicity data sets that include organisms in several trophic levels, organisms with different ecosystem functions, and groups of physiologically similar organisms are useful for characterizing toxicity profiles. In the case of some substances, particularly newly registered pesticides, toxicity data are often limited to the basal data set required for registration and measured exposure data may not be available at all. Fortunately, relatively large data sets were available for some of the pyrethroids. In these cases, groups of organisms could be assessed separately on the basis of a knowledge of mode of action, susceptibility, and toxicokinetics of the pyrethroid.

Key properties of the pyrethroid insecticides

The synthetic pyrethroid insecticides are widely used for pest management in both agriculture and public health. They have low toxicity to mammals and birds (LD50s generally > 1,000 mg/kg) but are highly toxic to insects as well as some

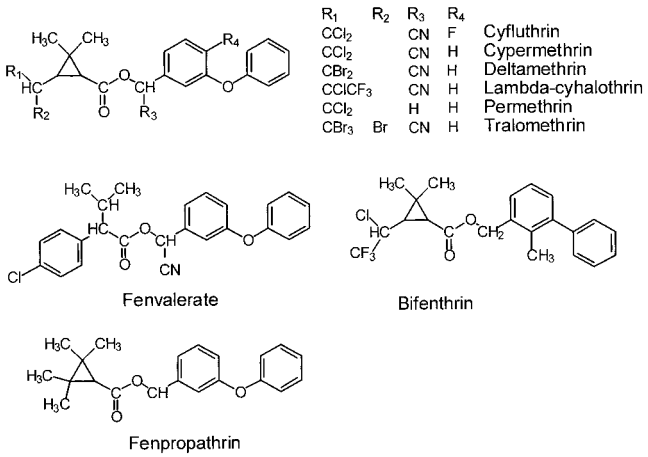

Fig. 1. Structure of the pyrethroids used in cotton (from [13]).

aquatic organisms, particularly aquatic insects (LC50s generally < 10,000 ng/L) [20]. Although the synthetic pyrethroids are generally considered to have low environmental persistence (water column $t_{1/2} < 4$ d), they have longer environmental half-lives than the natural products from which they were developed ($t_{1/2} < 8$ h in water, foliage, and so on), thus increasing their utility in agricultural use patterns [21]. Their low toxicity to mammals and birds also offers distinct advantages when they are used in agriculture but their toxicity to aquatic arthropods may present an environmental hazard if exposures are sufficiently great. Characterizing the toxicity of these insecticides in the context of ecological risk assessment requires consideration of some of their key physical and biological properties. Several reviews of the environmental properties and effects of pyrethroids have been conducted [2,3]. This paper is a synthesis of published and other toxicity data with a special focus on the cotton pyrethroids and on characterization of the toxicity data for aquatic organisms using distributional approaches.

As a class, the pyrethroid insecticides (Fig. 1) have relatively low water solubility (1,000–10,000 ng/L [13]) and high lipid solubility. This results in a high octanol–water partition coefficient (>10^5 [22]) and a relatively great potential for bioconcentration into organisms from surrounding matrices such as water. Although pyrethroids may bioconcentrate in organisms, depuration is also rapid and bioaccumulation through the food chain is not a significant route of exposure [2].

Mechanisms of action

The mechanism of action of the pyrethroids is through the nervous system. Their primary mode of action is through interference with ion channels in the nerve axon, resulting in hyperactivity of the nervous system with subsequent lack of control of normal function [21]. Two types of modes of action have been observed in mammals. That associated with the type I pyrethroids (non–cyano-, non–halogen-substituted pyrethroids, e.g., pyrethrum) is characterized by tremors (the T syndrome), whereas that associated with the type II pyrethroids (halogen-substituted acid moiety and cyano-substituted alcohol moiety) is characterized by choreoathetotic writhing and salivation. The type II pyrethroids seem to have a primary mechanism of action at the presynaptic membrane that involves increased release of synaptic vesicles through an effect on voltage-dependent calcium channels. The symptomology of poisoning by type I and type II pyrethroids in nonmammals

is not as distinct but similar depletion of presynaptic vesicles has been observed in insects [21]. Symptoms of poisoning appear rapidly for all pyrethroids. The rapid onset of poisoning and the lack of persistence of the pyrethroids in the environment increase the importance of acute toxicity data for assessing the potential for environmental effects.

In addition to their action in the nervous system, pyrethroids have been reported to interfere with certain ATPase enzymes associated with maintaining ionic concentration gradients across membranes [23]. This has been speculated to increase the sensitivity of freshwater aquatic organisms to these insecticides [20] through the addition of osmotic stress. This has also been suggested as the reason why fenvalerate is more toxic at median (isotonic) salinities in euryhaline species than at either high or low salinities [24].

In general, susceptibility to pyrethroids is dependent on sensitivity at the site of action and toxicokinetics. Included in the latter are bioavailability and rates of biological transformation. Haya [25] suggested that biotransformation may play a role in differential toxicity of pyrethroids to fish. This same mechanism may explain the general lower sensitivity to pyrethroids of fish compared to arthropods.

Isomer-specific toxicity

As for many substances with receptor-mediated mechanisms of action, different stereoisomers of the pyrethroids have different potencies. For example, the fenvalerate molecule can exist in four different optical isomeric forms, each of which has different biological properties (2*R*,α*R*; 2*R*,α*S*; 2*S*,α*R*; 2*S*,α*S*). The 2*S*,α*S* isomer is considerably more toxic than the 2*S*,α*R* and the two 2*R* isomers [26]. This has been exploited in the stereoselective synthesis of an enriched mixture known as esfenvalerate, which contains about 90% of the 2*S*,α*S* isomer and has greater efficacy against insect pests. The toxicity data set for fenvalerate was much larger than that for esfenvalerate. However, for five organisms, it was possible to compare the toxicity of the isomer-enriched and the nonenriched form. For *Daphnia magna*, bluegill sunfish (*Lepomis macrochirus*), and rainbow trout (*Oncorhynchus mykiss*), tests on the two isomers were conducted in different laboratories and at different times. Thus, these data are subject to interlaboratory and interstrain variability. In two studies, the toxicities of esfenvalerate and fenvalerate were evaluated concurrently and on the same strain of fish. These were the Australian crimson-spotted rainbow fish (*Melanotaenia fluviatilis*) [27] and the fathead minnow (*Pimephales promelas*) [26]. Esfenvalerate was more toxic to rainbow fish (twofold at 96-h exposure) and to fathead minnows (3.3-fold at 48 h) than was fenvalerate. The other results were equivocal, with essentially similar toxicity observed in *D. magna*; esfenvalerate was observed to be about 2.5 times less toxic in bluegill sunfish and about four times more toxic in rainbow trout. Bradbury et al. [26] also measured the toxicities of all four isomers by intraperitoneal injection in bluegill sunfish and showed that the 2*S*,α*S* enantiomer was 5.6 times more toxic than technical fenvalerate. Intraperitoneal injection exposure is not directly comparable to waterborne exposure because the toxicokinetics in the organism may be different and the 2*S*,α*S* enantiomer racemizes, albeit slowly, to the 2*S*,α*R* form in water; however, the greater toxicity of esfenvalerate was confirmed. Compared to intertest differences in toxicity and the range of toxicity between species, these differences are small. For this reason, data for esfenvalerate and fenvalerate were combined for the purpose of determining the distribution of toxicity.

MATERIALS AND METHODS

The basic approach to characterizing the toxicity of each of the pyrethroids was to compile all of the available data for aquatic species into a cumulative frequency distribution. For the purposes of characterizing the toxicity profile, the distribution was described by a linear regression of the log-probability–transformed data. Toxicity data for the pyrethroids were obtained from the U.S. Environmental Protection Agency Pesticide Toxicity Database (Oneliner Database [28]), from the open scientific literature, and from data supplied by the registrants (Pyrethroid Working Group members). For the U.S. Environmental Protection Agency Pesticide Toxicity Database, only data from core and supplementary studies were used. These raw data are not included in this paper but can be accessed at www.setac.org.

The acute toxicity data consisted of LC50 and EC50 measurements. For the purposes of this analysis, effective concentration (EC) and lethal concentration (LC) were treated similarly. The EC values in aquatic arthropods and insects are normally considered equivalent to LC values because the assay endpoint is immobility, an endpoint that either is, or will lead to death. The EC values in other organisms such as the oyster (*Crassostrea* spp.) may be based on shell deposition in larvae or inhibition of growth as measured by number of cells in algae. Combining these types of endpoints with those based on lethality may bias distributions of data; however, in this case, these data were excluded from analyses because of great insensitivity of these organisms or the use of concentrations well above the solubility limit (see additional discussion below). Although the suggestion has been made that lower (benchmark) effect levels such as the LC10 or the LC5 may be more appropriate for characterizing toxicity in valued ecosystem components such as fish [8], the LC/EC50 is usually the only datum available. This was the case for almost all of the pyrethroid data sets, and, in the absence of slope of the concentration–response line, other intercepts could not be calculated. A number of exposure time periods are commonly used for laboratory toxicity testing of aquatic organisms. The data used in this analysis were derived from acute assays conducted over periods from 24 to 96 h. Because the pyrethroids are rapid-acting insecticides with high K_{OW}s, uptake and expression of toxicity in aquatic organisms is rapid. The relatively short persistence of pyrethroids in the water column [2,4,29] also supports the use of acute toxicity data. Where toxicity in a single study was reported at more than one time period, only the longest time $\leq$96 h was used in the analysis.

Where sufficient acute toxicity values were available, data for arthropods and for fish were analyzed separately. As with many other pesticides, pyrethroids were developed as insecticides and would be expected to be more toxic to arthropods than to other organisms. In addition, separation of data into major groups is a useful technique for differentiating the assessment of risks in organisms with different potential for recovery. For example, fish may not be able to tolerate high return frequencies of adverse effects to the same degree as other groups, such as arthropods, whose populations can recover more rapidly.

Results from some toxicity assays, particularly those conducted with nonsusceptible organisms such as molluscs and algae, reported effect measures well in excess of the water

Table 1. Regression coefficients and intercepts for the acute toxicity data for the pyrethroids

	$y = ax + b$[a]			Regression intercepts (ng/L)[b]				
Pyrethroid	*a*	*b*	r^2	10%	5%	20%	50%	*n*[c]
Lamda-cyhalothrin	0.96	2.76	0.70	10	<4	29	220	9
Deltamethrin[d]	0.73	3.04	0.96	9	3	35	510	21
Bifenthrin	0.75	2.83	0.96	15	<3.8	58	770	12
Cyfluthrin[e]	0.71	2.97	0.95	12	<4	48	750	9
Tralomethrin	2.05	−1.38	0.84	<310	<310	500	1,300	6
Cypermethrin[d]	0.85	2.85	0.98	10	4	34	330	58
Arthropods	1.10	2.84	0.98	6.4	3	16	95	42
Vertebrates	1.73	−0.75	0.83	380	<230	690	2,100	17
Permethrin[d]	0.89	1.73	0.97	180	68	550	4,900	64
Arthropods	1.07	1.70	0.96	76	35	200	1,200	36
Vertebrates	1.31	−0.48	0.88	1,600	850	3,500	15,000	24
Fenvalerate	1.04	2.08	0.96	37	17	98	630	37
Arthropods	0.93	2.88	0.90	8	3	24	200	16
Fish	1.28	0.93	0.87	150	80	340	1,600	20
Fenpropathrin	1.12	1.06	0.90	240	114	600	3,400	13

[a] These values are transformed into units of log and probit for the purposes of regression and backtransforms were used to calculate intercepts.
[b] Intercepts are rounded to two significant figures.
[c] Number of data points used in the regression.
[d] Species with lethal concentration/effective concentration values above the limit of water solubility were excluded from the regression.
[e] Two species of algae were excluded from the regression.

solubility of the pyrethroids. For distributional analysis of data for all organisms, these data were omitted from regressions of the cumulative frequency distributions but were included in the calculation of ranks. The likelihood that these concentrations would ever be exceeded is extremely small and they are thus of minimal significance in the risk assessment process.

Some of the toxicity data were obtained from tests with formulated products. Toxicity data for formulated products were generally not very different from those for the technical material and, for this reason, they were included in the data sets. In all cases, the effect concentration was converted to active ingredient to allow for combination and comparison.

Where data from multiple studies on the same species were available, the recommendation has been made that the datum for the most sensitive life stage be used to represent that species in the distribution [9]. However, in many cases, information on exact life stage tested was not available. Thus, for multiple data for the same species, the geometric mean toxicity values were used to represent the species in the distribution. Although the lowest toxicity value could have been used as a conservative estimate of toxicity, use of the geometric mean results in a relatively conservative combination of data from different tests and allows all the data to be used in the distributions without assigning greater weight to species with more data or to one particular test. In some cases, particularly for insensitive organisms such as algae and molluscs, toxicity values were reported as greater than a certain concentration. These data were included in the plots for all organisms, even though they were likely lower than the true toxicity value. However, as discussed above, the concentrations were above the maximum solubility for the pyrethroids and were excluded from the regression.

Plotting positions were calculated from the formula $100 \times i/(n + 1)$ [30], where i is the rank of the datum and n is the total number of data points in the set, and are expressed as percentages. Data were plotted using a log-normal transformation and linear regressions were performed with the aid of the SigmaPlot 5 graphics package [31]. Although a number of other models may produce a better fit for some data sets [32], use of the log-normal model for characterizing toxicity distributions has been recommended [33–35] and is supported by observations in other studies [14–18].

The 10th centile of the toxicity distribution of a substance may be used as a convenient working criterion (assessment measure) for characterizing toxicity. From a theoretical point of view, any measure (the 5th, 10th, 20th, or 25th centile) could be used for assessment purposes, provided that this measure can be validated against a knowledge and understanding of ecosystem structure and function, or calibrated in tests conducted in microcosms or in the field. The 10th centile of LC50 data has been observed to be conservative in other situations where this criterion has been compared to responses in mesocosms [14,17] and is specifically addressed for pyrethroids in an accompanying paper [4]. The 10th centile was used as the primary assessment measure; however, several other centiles values were calculated for comparison.

RESULTS

Toxicity distributions

For all the cotton pyrethroids except tralomethrin, more than nine toxicity values were available for analysis. In these cases, centiles were calculated from the regression lines. The 10th centile for tralomethrin is considered less reliable because it was estimated by extrapolation. Therefore, the 10th centile for tralomethrin was reported as less than the lowest toxicity datum (Table 1); however, this number was not very different from the extrapolated 10th centile intercept. Where data sets were small (bifenthrin, cyfluthrin, and lambda-cyhalothrin), centiles below the lowest observed toxicity value were estimated by extrapolation and are presented as less than the lowest observation in the data set. Although these centiles may be less robust as a result, all the centiles followed a rank that would be expected from their known mode of action (see below). The plotting positions calculated above are dependent on the number of data points in the data set. For small data sets, the slope of the distribution is flatter, thereby giving more conservative (lower) centiles below 50%. However, one or two

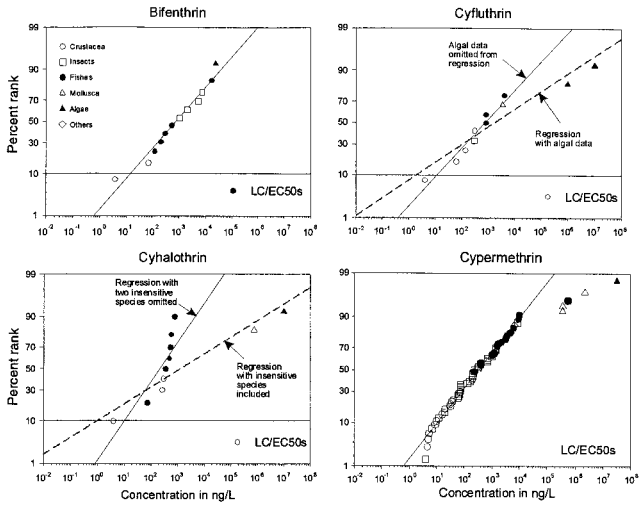

Fig. 2. Distribution of acute toxicity values for bifenthrin, cyfluthrin, lambda-cyhalothrin, and cypermethrin in aquatic organisms.

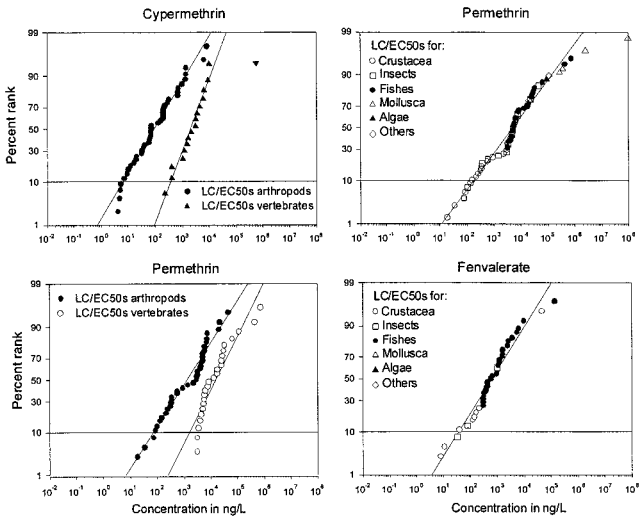

Fig. 3. Distribution of acute toxicity values for cypermethrin in aquatic arthropods and vertebrates, permethrin in aquatic organisms, permethrin in arthropods and vertebrates, and fenvalerate in aquatic organisms.

outlier organisms, such as one very sensitive or very insensitive organism, will also distort the distribution to cause the same effect. This outlier effect is even more pronounced with small data sets such as these.

Bifenthrin, cyfluthrin, and lambda-cyhalothrin. For bifenthrin (Fig. 2 and Table 1), the most sensitive organism was the mysid shrimp (*Americamysis bahia*) and the least sensitive was the *Cassostrea* spp. The 10th centile intercept was 15 ng/L. Insufficient data were available to assess arthropods and fish separately. The complete cyfluthrin data set (Fig. 2) had 11 data points and, once again, the most sensitive organism was *A. bahia*. The 10th centile intercept was 2 ng/L (Fig. 2). When the two insensitive organisms (the algae *Scenedesmus subspicatus* and *Selenastrum capricornutum*; Fig. 2) were omitted from the analysis (the reported EC50 values were greater than the highest concentration tested and in excess of the maximum water solubility) the 10th centile intercept was 12 ng/L (Fig. 2 and Table 1). This value is judged to be a better characterization of the toxicity distribution. The complete data set for lambda-cyhalothrin (Fig. 2) consisted of 11 data points. The most sensitive organism was *A. bahia* and the least sensitive were the oyster and *S. capricornutum*. These latter two effect concentrations were in excess of the maximum water solubility. Omission of these two data points from the regression gave a 10th centile intercept of 10 ng/L (Fig. 2 and Table 1), which is judged to be a better characterization of the toxicity distribution.

Cypermethrin. Cypermethrin (Fig. 2 and Table 1) gave a 10th centile intercept of 10 ng/L when all organisms were considered. The arthropods-only group (Fig. 3 and Table 1) gave a 10th centile intercept of 6.4 ng/L, whereas, for vertebrates, the intercept was 380 ng/L. As discussed above, fish would be expected to be less sensitive to insecticides than arthropods. Most of the organisms in the data set were freshwater organisms and a separate analysis of freshwater and saltwater organisms was judged to be not appropriate. Several data points on the distribution in Figure 3 were from very insensitive organisms (algae and a fish) and the reported concentrations were in excess of the water solubility of cypermethrin. These data were omitted from the regression but are presented on the graphs.

Permethrin. The distribution of permethrin toxicity to all organisms (Fig. 3 and Table 1) and toxicity to arthropods and vertebrates (Fig. 3 and Table 1) gave 10th centile intercepts of 180, 76, and 1,600 ng/L, respectively. The toxicity distributions for arthropods and fish (Fig. 3) were clearly separated by a factor of about 20, again illustrating the generally lower sensitivity of fish to the pyrethroids. In the distribution of toxicity to all organisms the least susceptible organisms were molluscs and the two most sensitive organisms were Crustacea, one of which was *A. bahia*. The separate analysis of freshwater and saltwater organisms in this data set (Table 2) showed a distinct difference in the toxicity distribution of the arthropods. For risk assessments in freshwater, the 10th centile intercepts of 170 and 1,400 ng/L, respectively, for arthropods and fish are judged to be more appropriate assessment measures.

Fenvalerate and esfenvalerate. The toxicity distribution for combined data for fenvalerate and esfenvalerate in all organisms had a 10th centile of 37 ng/L (Fig. 3 and Table 1) with the most sensitive organism being *A. bahia* and the two least sensitive being *Uca pugilator* and *Tilapia mossambica*. The 10th centile intercepts for arthropods and fish (Fig. 4) demonstrated 10th centiles of 8 and 150 ng/L, respectively. The differences between the toxicity distributions for arthropods and fish were similar to those observed for other pyrethroids.

Tralomethrin, fenpropathrin, and deltamethrin. The data set for tralomethrin consisted of only six measurements. The 10th centile for the tralomethrin toxicity distribution (Fig. 4 and Table 1) was <310 ng/L. The most sensitive organism was *D. magna* and the least sensitive was *Cyprinodon variegatus*. The 10th centile for fenpropathrin toxicity data was 240 ng/L and the data set consisted of 13 data points (Fig. 4 and Table 1). The most sensitive organism was again *A. bahia* and the least sensitive was the oyster (*Cassostrea virginia*). The deltamethrin distribution (Fig. 4 and Table 1) consisted of 24 data points with the most sensitive organisms being the lobster (*Homarus americanus*) and *A. bahia*. The least sensitive organisms were all molluscs (Fig. 4) with reported LC50s in excess of 10^8 ng/L (well above the maximum water solubility). When these organisms were omitted from the regression, the data demonstrated a 10th centile intercept of 9 ng/L. The large difference between the toxicity of tralomethrin

Table 2. Regression coefficients and intercepts for the acute toxicity data for permethrin and fenvalerate in freshwater and saltwater organisms

Group	$y = ax + b$[a]			10th centile regression intercept (ng/L)[b]	n[c]
	a	b	r^2		
Permethrin					
All saltwater organisms	0.63	2.88	0.97	22	18
All freshwater organisms	0.84	1.75	0.88	220	48
Saltwater arthropods	1.07	2.53	0.96	13	9
Saltwater fish	1.49	−0.98	0.90	1,400	7
Freshwater arthropods	1.22	0.99	0.94	170	25
Freshwater vertebrates	1.18	0.03	0.86	1,400	18
Fenvalerate					
All saltwater organisms	0.97	2.33	0.93	27	20
All freshwater organisms	0.95	2.30	0.91	31	17
Saltwater arthropods	0.59	3.67	0.94	1	7
Saltwater fish	1.99	−0.98	0.97	230	12
Freshwater arthropods	1.85	0.76	0.97	40	9
Freshwater fish	0.92	1.80	0.90	120	8

[a] These values are transformed into units of log and probit for the purposes of regression and backtransforms were used to calculate intercepts.
[b] Intercepts are rounded to two significant figures.
[c] Number of data points used in the regression.

and deltamethrin (its degradate) in *A. bahia* is possibly explained by a lack of activation of tralomethrin in the flow-through bioassay system.

Susceptibility of freshwater and saltwater organisms

No differences in distributions of toxicity in saltwater and freshwater organisms were observed in the case of atrazine [14]. For permethrin and fenvalerate, sufficient data were available to test this hypothesis. For permethrin, the distributions of toxicity for all freshwater and all saltwater organisms were different, especially in the region of the lower centiles. In addition, the distributions had different slopes (Fig. 5 and Table 2). When data for arthropods and vertebrates were separated (Fig. 5 and Table 2), it became obvious that the difference in intercept for the grouped data was caused by the difference in the susceptibility of the saltwater and freshwater arthropods and a lack of difference in the vertebrates. For fenvalerate (Fig. 5 and Table 2), differences were not as distinct. The distributions for all saltwater and all freshwater organisms were similar but, when data for arthropods and fish were analyzed separately, the differences in the distributions became apparent (Fig. 5 and Table 2). Saltwater and freshwater fish demonstrated similar distributions; however, the 10th centile for the arthropods differed by a factor of about 40, with the saltwater organisms being more susceptible. The saltwater mysid shrimp *A. bahia* was, in many cases, the most sensitive arthropod to the pyrethroids; however, the *Cassostrea* spp., another saltwater species, was often among the least sensitive organisms. Thus, a broad generalization that all saltwater organisms are more sensitive to pyrethroids is not justified; however, this does seem to be true for the arthropods. The difference in response between saltwater and freshwater arthropods may be the result of differences in pharmacokinetics or changes in bioavailability, salinity stress [24], or inclusion of less sensitive insects in the freshwater arthropod group only. Although the exact mechanism for this is not clear, it does suggest that, for these pyrethroids, risks to freshwater and saltwater arthropods should be assessed separately.

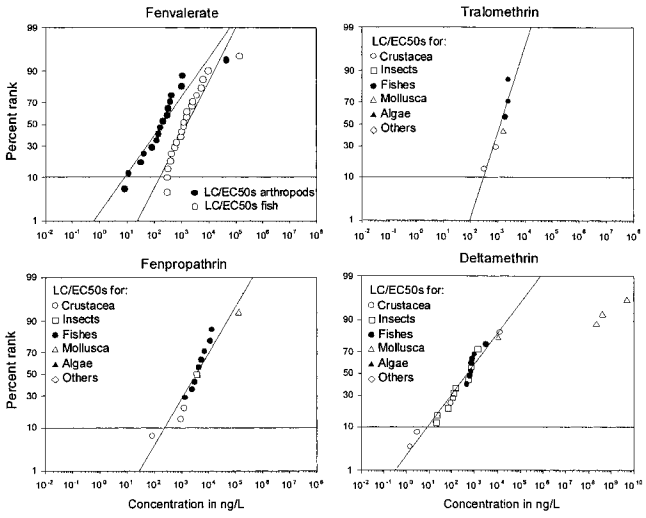

Fig. 4. Distribution of acute toxicity values for fenvalerate and esfenvalerate in arthropods and fish, and tralomethrin, fenpropathrin, and deltamethrin in aquatic organisms.

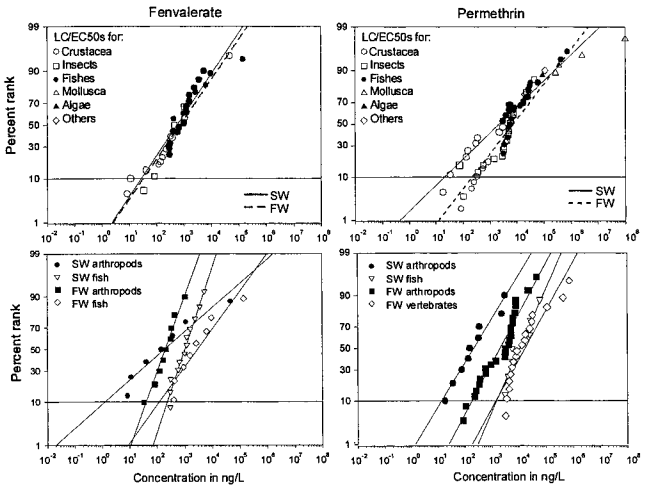

Fig. 5. Distribution of acute toxicity values for permethrin and fenvalerate in freshwater and saltwater aquatic organisms.

The data sets for the other pyrethroids were judged to be too small to be assessed in this way. Therefore, in the absence of information suggesting that saltwater organisms are inherently more susceptible to these pyrethroids, it was assumed that the saltwater organisms were part of the continuum of responses and, for the purposes of the distributional analysis of these pyrethroids, data from saltwater and freshwater organisms were not separated. In cases where risks to freshwater environments were being assessed, use of the combined data would add a measure of conservatism to the characterization of toxicity.

Chronic toxicity data

Some chronic toxicity data were available in the literature and from studies submitted by registrants. Exposure periods were varied, ranging from 10 to 240 d. The chronic toxicity data sets were smaller than the acute data sets and were judged to be unsuitable for distributional analysis. Acute-to-chronic ratios ranged from 2 to 415, with an arithmetic mean of 44 for the cotton pyrethroids.

Toxicity characterization of the pyrethroids as a class of compounds

The pyrethroids have similar mechanisms of action as well as similar physicochemical properties. As a result, they show similar behavior with respect to their spectrum of toxicity to target and nontarget organisms as well as with respect to their movement and fate in the environment. The toxicity values for the pyrethroids were generally consistent, with the most sensitive organism being *A. bahia* and the least sensitive being the oyster. Fish also were consistently less susceptible than arthropods. This raises the question of whether they have similar enough toxicologic properties to be treated as a group for risk assessment purposes. With the exception of tralomethrin, the distributions of toxicity had similar slopes, suggesting that the extent of toxicity in a range of aquatic organisms is similar; however, differences existed in the positions of the distributions, as evidenced by their 10th centile intercepts (Table 1). The pyrethroids do have different recommended field rates of application that are related to their efficacy [2], and a plot of field rate versus 10th centile concentration showed a trend for the high-use (permethrin and fenpropathrin) and the low-use (deltamethrin, cyhalothrin, fenvalerate, cyfluthrin, bifenthrin, and cypermethrin) pyrethroids (Fig. 6). The exception to this trend is tralomethrin, which has a high 10th centile for its toxicity distribution but a low field application rate. The apparent low toxicity to aquatic organisms may be an artifact of the use of flow-through or static-renewal bioassays, where insufficient time is available for dehalogenation of tralomethrin to the more toxic deltamethrin. Because of its low application rate (similar to that for deltamethrin), a risk assessment based on the other pyrethroids would be protective of tralomethrin.

Using one of the pyrethroids as a reasonable worst-case surrogate for the other pyrethroids may be a useful risk assessment strategy. Cypermethrin is a good candidate pyrethroid to fulfill this role. The data set for cypermethrin was large and, for all organisms and for arthropods alone, cypermethrin had among the lowest 10th centiles for its toxicity distributions (Table 1). It also had a relatively high application rate (Fig. 6) compared to the other pyrethroids (excepting permethrin and fenpropathrin). Assuming that concentrations in nontarget water bodies are directly proportional to the field application rate and that differences in environmental fate are relatively minor when compared to the 96-h exposure concentrations used in toxicity bioassays, a risk assessment based on the toxicity distribution of cypermethrin and its likely concentrations in the environment would be conservative for all the other pyrethroids. Substitution of the other pyrethroids at lesser use rates would result in smaller exposure concentrations and the greater 10th centiles for the distributions of toxicity would result in smaller exceedence probabilities.

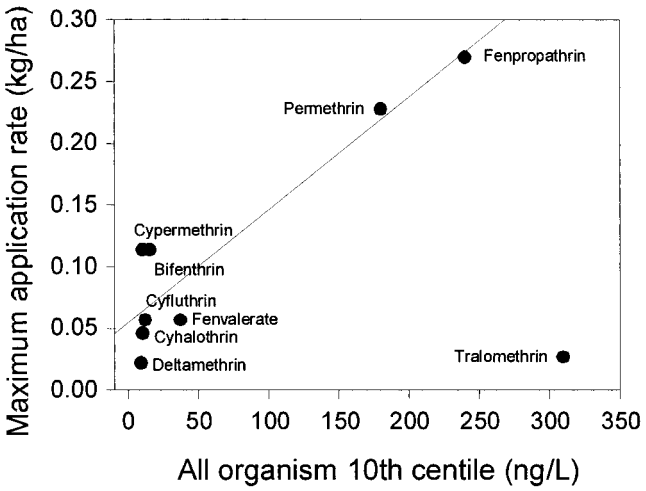

Fig. 6. The relationship between 10th centiles of toxicity distributions and maximum field rates for the cotton pyrethroid insecticides. Tralomethin was excluded from the regression because laboratory assays may not accurately reflect the toxicity of its activation product.

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